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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,232

03/24/2006

Menachem Rubinstein

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07/20/2009

MARTIN D. MOYNIHAN d/b/a PRTSI, INC.

P.O. BOX 16446

ARLINGTON, VA 22215

EXAMINER

PAGONAKIS, ANNA

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/560,232	Applicant(s) RUBINSTEIN ET AL.	
	Examiner ANNA PAGONAKIS	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 6-46 is/are pending in the application.
- 4a) Of the above claim(s) 12-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 6-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2 sheets, 2/2/2009; 1 sheet, 5/28/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's amendment filed 3/16/2009 have been received and entered into the present application.

As reflected by the attached, completed copy form PTO/SB/08A (three pages total), the Examiner has considered the cited references.

Applicant's arguments filed 3/16/2009 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in

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question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The claims are drawn to a method of treating obesity comprising administering to an individual in need thereof a pharmaceutical composition comprising AS101.

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The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain).

As illustrative of the state of the art, the examiner cites:

(1) Lillioja et al. Free fatty metabolism and Obesity in Man: In vivo vs. In vitro comparisons. *Metabolism*, Vol. 35, No. 6, 1986, pp. 505-514.

(2) U.S. Patent 7,045,150.

The first reference, concluded that FFA is not available in vivo in proportion to the size of the triglyceride stores. The measures of fat cell lipolysis cannot be used to directly predict in vivo FFA metabolism (abstract). The data suggests that the fat cells were more than capable of releasing large amounts of FFA in obese subjects but apparently failed to do so in vivo. These results indicate that in obese subjects much of the increased fat store may not be accessible to the rest of the body. Furthermore, in vitro measurements of fat cell lipolysis cannot be used to directly predict in vivo fatty acid metabolism.

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U.S. Patent 7,045,150 teaches that AS101 enhances the cumulative weight gain and feed efficacy in poultry (column 1).

Both references teach for the unpredictability of the current invention. Reference (1) teaches that in vitro studies cannot in fact be relied upon for an accurate prediction for in vivo environments (Example 4). Reference (2) teaches the **opposite** of what is claimed by Applicant, specifically that AS101 induces weight gain.

2. The breadth of the claims

The claims encompass the treatment of obesity comprising AS101.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimens (*e.g.*, dosages, timing, administration routes, etc.) necessary to treat obesity, particularly in humans.

The direction concerning treating obesity in humans is not found in the instant specification, Applicant's merely state that ob/ob mice are predictive candidate for human obesity. No formulations or dosages or modes of administration are discussed.. There are no guidelines for determining the doses needed to treat a condition of this sort.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed genus of compounds could be predictably used as a treatment for obesity as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in

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return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

Determining if any particular claimed compound would treat any particular cancerous disease state would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or to testing in an assay known to correlate to clinical efficacy of such treatment. This is undue experimentation given the limited guidance and direction provided by Applicants. As noted *supra*, even *in vitro* and *in vivo* assays do not always correlate to efficacy in humans and are not generally predictive of clinical efficacy.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Response to Applicant's Remarks

Applicant alleges that the remarks provided in the response are done so under the assumption that the Examiner's rejection relates to a method of treating obesity comprising administering the elected species. The Examiner guides Applicant to page 3, last two lines, of the Office Action mailed on 9/17/2008 which clearly states "The claims are drawn to a method of treating obesity comprising administering to an individual in need thereof a pharmaceutical composition comprising AS101." Therefore, it is not clear to the Examiner why Applicant is making assumptions when the Action clearly provides this statement as drawn to the nature of the invention. *Applicant alleges that the instant application provides experimental evidence of two in vivo experiments.* The Examiner agrees that two in vivo experiments have been disclosed in the specification. *Applicant alleges that the in vitro results presented in the specification are related to reduced adipocyte generation whereas those of the reference Lilloja et al. is drawn to lipolysis measurements and therefore are unrelated.* Applicant fails to advance any specific reasons or evidence, aside from Counsel's own allegation, in support of this position.

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This assertion by Counsel is an unsupported allegation and fails to take the place of evidence in the record. Statements of this nature are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, “The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)”. *Applicant allege that the ob/ob mouse model is an art-recognized model of obesity.* Though this is noted, Applicant has only studied one model which is not predictive for different routes of obesity pathogenesis. Friedman et al. teach that there are three general ways in which alterations of the leptin regulatory loop could lead to obesity such as a) failure to produce leptin, as occurs in ob/ob mice, would result in obesity, as would b) inappropriately low leptin secretion for a given fat mass. In the latter case, the fat mass would expand until 'normal' leptin levels are reached, resulting in obesity. Finally, obesity could result from relative or absolute insensitivity to leptin. In general, high plasma leptin levels are evident in obese rodents and humans. In a subset of cases, obesity is associated with normal levels of leptin (page 766, column 2). Applicant has not addressed other types of pathogenesis of obesity in their experiments. *Applicant states that U.S. 7,045,150 teaches the growth of immature poultry which is in contrast to a method of treating obesity.* The Examiner requests Applicant re-evaluate the relevance of this reference. The reference was cited as art teaching that in fact the claimed compound leads to weight gain *not* weight loss. *Applicant alleges that the weight gain of U.S. 7,045,150 occurs in a growing immature individual unrelated to weight gain.* This is not persuasive. Applicant is guided to the breadth of their own independent claim which is drawn to the administration of an individual. According to Applicant's own statement, poultry is considered an individual. *Applicant alleges that U.S. 7,045,150 does not teach that the poultry are obese.* Again, the Examiner states that the purpose of use of the reference is to teach that the art teaches the opposite effect than that claimed by Applicant (i.e. induction of weight gain).

Conclusion

No claim is found to be allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614